Docket No.: 21059/0206916-US0
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Bakulesh Khamar et al.

Application No.: 10/565,211 | Confirmation No.: 9175

Filed: October 30, 2006 | Art Unit: 1645

For: PROCESS FOR MANUFACTURING PHARMACEUTICAL COMPOSITION COMPRISES OF MYCOBACTERIUM W IN THE TREATMENT OF ASTHMA (OBSTRUCTIVE LUNG DISEASE) | Examiner: R. P. Swartz

DECLARATION OF DR. JAMES P. LAMBERTI UNDER 37 C.F.R. 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Dr. James P. Lamberti, declares under penalty of perjury under the laws of the United States of America as follows:

(1) I graduated from the University of Pennsylvania School of Medicine in 1980. I completed an internship and residency in Internal Medicine at the Hospital of the University of Pennsylvania. I completed a fellowship in Pulmonary Medicine at Boston University School of Medicine in 1985. I am board-certified in Internal Medicine and Pulmonary Medicine and have been licensed to practice medicine in the state of Virginia since 1985. I have practiced pulmonary medicine since 1985, employed by Northern Virginia Pulmonary and Critical Care Associates, P.C. In light of my background, I consider myself to be an expert in pulmonary medicine and treatment of patients having pulmonary diseases.

(2) While I am not an inventor on the present application, I am familiar with the subject matter and claims of the present application. The assignee of the present application is Rajiv Indravadan Modi, who is the Managing Director of Cadila Pharmaceuticals Ltd. (herein after "Cadila"). I have been retained by Cadila to review this application, the Examiner's rejections, and prepare this declaration.

(3) I reviewed the Examiner's rejections in the Actions of October 16, 2007 and June 9, 2007. The Examiner rejected Claims 22-48 because the Examiner concluded that "the claimed subject matter was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or which it is most nearly connected, to make and/or use the invention." Specifically, the Examiner required information such as "the actual composition administered to the patients (whole cells, disrupted cells, cell fractions, etc.), the dosage administered, the route of administration, and the frequency of administration."

(4) I reviewed the '211 application in its entirety including the written description and the claims. I have also reviewed the accompanying Rule 132 declaration of Dr. Khamar. In this declaration, he provides further clarifications as to how the examples were reduced to practice by the inventors. The additional data in the Rule 132 declaration of Dr. Khamar are nothing more than minor details that someone practicing medicine or doing medical research would find routine and well-known in the field of medicine. The additional data in the Rule 132 declaration of Dr. Khamar supplements the specification, which clearly provides enough details to a person practicing pulmonary medicine or doing medical research to practice the invention of Dr. Khamar and his co-inventors.

(5) I conclude that one of ordinary skill in the art of the present invention, i.e., a pulmonary medicine specialist, at the time of the filing of the '211 application would have been able to practice the claimed invention after reading the application. Specifically, regarding the composition of the dosages, I note that Example 1 teaches several therapeutic compositions in which each dosage includes 0.1 ml of the therapeutic agent. Example 1 further teaches that compositions A, B, C and J contain heat killed whole cell Mycobacterium w, composition D contains extract of Mycobacterium

w after sonication (i.e., after cell disruption), and compositions E to I contain cell fraction extracted Mycobacterium w.

(6) As the Examiner's contention is that the specification does not teach "the actual composition administered to the patients (whole cells, disrupted cells, cell fractions, etc.), the dosage administered, the route of administration, and the frequency of administration," I prepared the chart shown below to determine what the application explicitly states in Examples 4 and 6, and identify gaps, if any, in the disclosure of the application based on the Declaration of Dr. Khamar, attached herewith.

Example	**Composition**	**Dosage**	**Route of Administration**	**Frequency of Administration**
Example 4 (as stated in the original application)	"Mycobacterium w"	Not explicitly stated	"intradermally"	Dosages given "at the interval of one week"
Example 4 (as clarified in the Declaration of Dr. Khamar)	Mycobacterium w as provided in Example 1A	0.2 ml per week initially followed by 0.1 ml per week	intradermally	Dosages given at the interval of one week
Example 6 (as stated in the original application)	"Mycobacterium w containing pharmaceutical compositions"	"0.1 ml"	Not stated	Dosages given "at the interval of one week"
Example 6 (as clarified in the Declaration of Dr. Khamar)	Mycobacterium w containing pharmaceutical compositions as provided in Example 1A	0.1 ml	Nebulizer	Dosages given at the interval of one week

(7) In short, both Examples 4 and 6 state that the composition contains "Mycobacterium w" but does not explicitly state "Mycobacterium w as provided in Example 1A." In addition, Example 4 does not explicitly state that the dosage was 0.2 ml per week initially followed by 0.1 ml per week and Example 6 does not explicitly state that the route of administration was through a nebulizer. Having identified these "gaps" in Examples 4 and 6, I now provide my analysis as an expert in pulmonary medicine, which is the field of this invention, as to why these "gaps" would have been obvious to me.

(8) Regarding the "gap" in composition, I notice that Examples 4 and 6 state that the compositions contain "Mycobacterium w" but does not explicitly state which composition of Example 1 was specifically used. However, Example 1 provides several compositions as Examples 1A to 1J. Thus, based my understanding of this art, I would recognize that Examples 4 and 6 could be carried out using any of Examples of 1A to 1C, which contain 0.5×10^9 heat killed Mycobacterium w, Example 1D, which contains 1×10^9 sonicated Mycobacterium w, Examples 1E to 1I, which contain 1×10^9 solvent extracted Mycobacterium w, or Example 1J, which contains 0.5×10^7 heat killed Mycobacterium w. The concentration of Mycobacterium w in Examples 1A to 1J is 0.5×10^7, 0.5×10^9 or 1×10^9. In light of Examples 1A to 1J, it would have been obvious to select a concentration of Mycobacterium w of 0.5×10^7 for patients who have a lower degree of respiratory impairment, to use a concentration of Mycobacterium w of 0.5×10^9 for patients who have a moderate degree of respiratory impairment, and to use a concentration of Mycobacterium w of 1×10^9 for patients who have a higher degree of respiratory impairment. In fact, as a first choice, I would select Example 1A having a concentration of Mycobacterium w of 0.5×10^9, as it is the first exemplary composition in the specification and because the concentration of Mycobacterium w of 0.5×10^9 falls within the upper and lower limits of concentrations of Mycobacterium w of 0.5×10^7 and 1×10^9 disclosed in Examples 1A to 1J. In short, based on the disclosure of the '211 application, it would have been obvious to me to select "Mycobacterium w as provided in Example 1A" having a concentration of Mycobacterium w of 0.5×10^9 in the compositions of Examples 4 and 6.

(9) Regarding the "gap" in dosage in Example 4, I notice that each one of Examples 1A to 1J states, "Each dose of 0.1 ml of therapeutic agent." Typically, the intradermal dose of a medication is 0.1 ml. It is common in pulmonary medicine to utilize a "loading" or priming dose of a medication followed by a maintenance dose. As a practitioner of pulmonary medicine, I consider it routine to give a dosage of 0.2 ml, followed by a dosage of 0.1 ml, when the dosage is administered intradermally, as was done in Example 4 according to Dr. Khamar's Declaration.

(10) Regarding the "gap" in the route of administration in Example 6, I notice that Example 4 states that the patient "was given Mycobacterium w intradermally at the interval of one week," and that pages 2-3 of the specification teach that asthma medications may be inhaled or taken orally. In fact, it is well-known that pulmonary medications can be administered intradermally, inhaled through a nebulizer, or taken orally. Furthermore, it is well known in pulmonary medicine that all of the three routes are interchangeable and can provide an effective therapy. The specific route of administration depends mostly on patients' choice, rather on any other factors. Thus, even though Example 6 does not explicitly disclose that Mycobacterium w was administered using a nebulizer as explained in Dr. Khamar's Declaration, this "gap" is not a flaw in the specification that would prevent me or other pulmonary medicine specialists from practicing this invention as I often use different routes based on patients' choice as these routes are interchangeable.

(11) Based on the cited specific compositions, dosages, routes of administration, and frequencies of administration in the '211 application, I conclude that one of ordinary skill in the art at the time of the filing of the '211 application having read the application would have been able to practice the claimed invention without undue experimentation. One of ordinary skill in the art of pulmonary medicine would understand (1) that the appropriate therapeutic dosage is typically 0.1 ml of Mycobacterium w, but could also be twice this dosage for patients with a higher degree of respiratory impairment, (2) the dosage may include whole cells, sonicated cells, or extracted cell fractions, (3) the composition could be administered intradermally or by nebulizer approximately once per week, and (4) treatment could be continued from four weeks to three months, or longer or shorter depending on the response exhibited by the patient to the treatment.

(12) I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct. Executed at Oakton, Virginia, United States of America, on this 31 day of December 2007.

James P. Lamberti, M.D.